## REMARKS/ARGUMENTS

### Status of claims

Claims 1 and 15 have been amended. Support for the amendment of claims 1 and 15 may be found in the specification, for example, at page 44, lines 11-18. Claim 1 has also been amended to provide proper antecedent basis for later dependent claims. Thus, no new matter has been added. Reconsideration is respectfully requested in light of the remarks which follow.

### New grounds of objection - antecedent basis

Claims 1, 5-13, 15, 17, 19, 20, and 22 stand objected to as allegedly lacking proper antecedent basis in the specification for the recitation of a method of screening for a modulator of RDGC GPCR phosphatase activity, in which the method comprises "providing a second sample comprising rhodopsin G protein coupled receptor and a mutant Drosophila RDGC phosphatase and comparing the level of Drosphila RDGC phosphatase in the first and second sample to thereby detect RDGC GPCR phosphatase activity and to detect a modulator of RDGC GPCR phosphatase activity." *See* Office Action at page 3. This limitation in current claim 1 was present in originally filed claim 14. However, the Examiner questions whether there is proper antecedent basis for these limitations. *See* Office Action at page 3. Without conceding the Examiner's rejection, Applicants have amended claims 1 and 15 to remove these limitations from these claims, thus obviating this ground for rejection.

### New grounds of rejection under 35 U.S.C. § 112, first paragraph - written description

Claims 1, 5-13, 15, 17, 19, 20, and 22 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In making this rejection, the Examiner alleges that there is inadequate written description support for the recitation of the genus of "mutant" Drosophila RDGC phosphatases in the claims because "no mutant Drosophila RDGC phosphatases have been sufficiently described in terms of their specific and complete chemical structure." *See* Office Action at page 6. Without conceding the Examiner's rejection, Applicants have amended claims 1 and 15 to remove recitation of the step

specifying the use of mutant Drosophila RDGC phosphatase from these claims, thus obviating this ground for rejection.

**Claim rejections under 35 U.S.C. § 112, second paragraph - definiteness**

Claims 1 and 5-13 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner has pointed to the recitation of "the rhodopsin" in claim 5 as lacking antecedent basis. Applicants have amended claim 1 to recite " a rhodopsin", thus providing claim 5 with antecedent basis in claim 1. Accordingly, Applicants respectfully request withdrawal of this ground for rejection.

**Claim rejections under 35 U.S.C. § 103**

Claims 1, 5-13, 15, 17, 19, 20, and 22 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Byk (PNAS, 93:1907-1911 (1993)) ("Byk") in view of Zuker (PNAS 93: 571-576 (1996)), Fang (U.S. Patent No. 5,693,488), and Steele (Cell, 69: 669-676 (1992)).

A. Legal standard for obviousness

The Supreme Court has affirmed the analysis set forth in *Graham* for the determination of obviousness. *See KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). Specifically, the Supreme Court, quoting from *Graham*, stated:

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. *Id.* at 1734.

Furthermore, the Court preserved the teaching, suggestion, and motivation (TSM) test, stating "[t]here is no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis", noting that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does." *Id.* at 1741; *see also*, USPTO memorandum on *KSR v. Teleflex*, dated May 3, 2007.

Thus, there continues to be a requirement that a motivation to combine the teachings must be explicitly and clearly stated by the Patent Office in making an obviousness rejection. The USPTO memorandum is in agreement, stating "[t]herefore in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed". *See* USPTO memorandum on *KSR v. Teleflex*, dated May 3, 2007.

Moreover, as set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations." All three elements set forth above must be present in order to establish a *prima facie* case of obviousness.

Thus, the *Graham* factors, including the use of objective evidence of secondary considerations to rebut a *prima facie* case of obviousness, as well as, a flexible use of the TSM test remains the framework to be followed for a determination of obviousness.

B. Teachings of the cited references

Byk is cited by the Examiner as allegedly disclosing a method that comprises the steps of: "i) providing a first sample of eye membranes containing wild type RDGC, ii) contacting the first sample with a test compound, iii) providing a second sample of eye membranes containing mutant RDGC, iv) contacting the second sample with a test compound, v) detecting Drosophila RDGC GPCR phosphatase activity in the first and second sample, and comparing the level of Drosophila RDGC GPCR phosphatase activity in the first and second sample, thereby identifying a modular of RDGC GPCR phosphatase activity." The Examiner alleges that calcium and arrestin as assayed in Byk constitute "test compounds". *See* Office Action at pages 8-9.

Furthermore, Zuker is cited by the Examiner as allegedly providing the motivation to identify additional molecules that effect the dephosphorylation and

phosphorylation of rhodopsin. Fang is cited by the Examiner as allegedly teaching methods of screening for mimetics of phosphatases. Steele is cited by the Examiner as teaching SEQ ID NO: 1. *See* Office Action at pages 9-11.

Thus, the Examiner alleges that it would have been *prima facie* obvious for one of skill in the art to have been motivated by the teachings of Zuker to use the experimental system of Byk to screen for the phosphatase mimetics of Fang, employing SEQ ID NO: 1, as taught by Steele.

C. Identification of allowable subject matter in the Office Action of February 16, 2006

Applicants thank the Examiner for helpfully pointing out the allowability over the prior art of claims directed to "methods of screening for modulators of RDGC phosphatase activity wherein the methods comprise exposing a first and second sample to a test compound and to RDGC phosphatase comprising the sequence of SEQ ID NO: 1, wherein the first sample comprises rhodopsin and the second sample comprises a mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus and comparing the level of RDGC phosphatase activity in the first and second sample to thereby identify a compound that modulates RDGC phosphatase activity" in the Office Action of February 16, 2006. *See* Office Action of February 16, 2006 at page 8.

However, the Examiner alleged that various aspects of the claim as recited above lacked written description, and thus, constituted new matter. In particular, while finding that the mutant rhodopsin itself was fully described in the specification, the Examiner stated that "the specification as originally filed does not appear to set forth the concept of comparing the results obtained with samples containing wild type rhodopsin to samples containing mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus, to thereby identify modulators of RDGC GPCR phosphatase activity." (Emphasis added.) *See* Office Action at page 3. Rather, the Examiner stated that "the specification teaches that the results obtained with rhodopsin and a test compound are compared to control samples or animals without the test compound." *See* Office Action at page 4. Thus, the Examiner states that the comparison is between phosphatase activity in a sample with a test compound versus the activity without the test compound.

Applicants have amended claim 1 (with corresponding amendments to claim 15) to recite:

"A method of screening *in vitro* for modulators of RDGC GPCR phosphatase activity, the method comprising the steps of:

(i) providing a first sample comprising a rhodopsin G protein coupled receptor and a Drosophila RDGC phosphatase comprising the sequence set forth in SEQ ID NO:1;

(ii) contacting the first sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity;

(iii) providing a second sample comprising a mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus as compared to wild type and a Drosophila RDGC phosphatase comprising the sequence set forth in SEQ ID NO: 1;

(iv) detecting a change in the level of Drosophila RDGC GPCR phosphatase activity in the first sample contacted with the compound, thereby detecting RDGC GPCR phosphatase activity; thereby detecting modulators of RDGC GPCR phosphatase activity;

wherein the test compound is a RDGC mimetic."

As amended, claims 1 and 15 no longer recite a method of screening that specifies a comparison of phosphatase activity in samples containing wild type versus mutant rhodopsin, but rather, these amended claims recite a screening method that requires comparing the phosphatase activity in a sample in the presence and absence of a test compound, which the Examiner has stated to be supported by the specification.

Applicants respectfully submit that claims 1 and 15, as amended, are allowable over the prior art because at a minimum, the references, alone and in combination, fail to teach or suggest the use of a mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus as a step in the screening for compounds which modulate RDGC GPCR.

Because the cited references, alone and in combination, fail to teach each and every element of amended claims 1 and 15, for at least this reason, a *prima facie* case of obviousness can not be established. Accordingly, Applicants respectfully request withdrawal of this ground for rejection.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

Gene H. Yee

Gene H. Yee
Reg. No. 57,471

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300

GHY:kk
61288828 v1